

tive action, but not until an opening large enough to receive a hen's egg had been produced. The granulation was rapid; the constitutional symptoms of gangrene soon disappeared, and the man recovered with a perfectly useless leg, since a hiatus of eight inches remained between the two extremities of the tibia. He was sent home on Oct. 12th, 1863, in good health, his term of service having expired.

DOUGLAS HOSPITAL, WASHINGTON, D. C.

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**ART. VIII.—*Observations upon One Hundred Cases of Intermittent Fever in which the Sulphate of Cinchonia was used as a Substitute for Quinia.*** By A. PAUL TURNER, M. D., one of the Physicians to the Howard Hospital and Infirmary for Incurables.

WHEN we consider the extremely limited regions to which the production of the desirable varieties of the Cinchona is confined, and the reckless destruction pursued in collecting it by those solely interested in an immediate pecuniary reward, and the utter neglect of the respective South American Governments to enforce the regulations necessary to its preservation, we may well feel assured that unless some available substitute for quinia be introduced, the supply is liable at any time to suddenly fail. So little interest in the subject is manifested in the regions from whence our supplies are now derived, that it is said in the collection arranged at the late International Exhibition at London, not a single specimen was placed there by the Spanish or South American States. In view of these facts, the British and Dutch Governments have been induced to establish nurseries for the cultivation of the Cinchona in their East India possessions. In carrying out the attempt, numerous difficulties are to be overcome, and it further remains to be ascertained, if even an apparent maturity be obtained, so far as all external characteristics are concerned, whether the bark possesses the full medicinal properties. To a certain degree the valued alkaloids in the Cinchona of the Indies may be in less quantity,<sup>1</sup> as the active resinoid principle of the hemp is almost wanting in those specimens cultivated elsewhere than the Indian Archipelago. Casting aside all this, we must admit that a considerable length of time will elapse, perhaps not less than twenty years, before a supply can be looked for from new sources, and an efficient substitute must, therefore, be procured, unless chemistry places at our disposal some method by which these desirable preparations can be directly formed. Notwithstanding we possess salicin, bebeerine, and the active principles of the oak, dogwood, and other indigenous plants, with copper, arsenic, etc. etc. of the mineral kingdom, all having more or less reputed antiperiodic properties, and useful in their

<sup>1</sup> [Recent investigations are said to show that the bark of the Cinchona trees raised in India is very rich in quinia.—EDITOR.]

proper places, yet it has always been desirable to secure one more energetic and certain in its action than those of the first class, without the well-known disadvantages attending the latter substances of not only being tardy in action, but requiring such care in administration as to cause their claims to be repudiated by many.

As early as 1821, when Pelletier and Caventou discovered that in Peruvian bark there existed another alkaloid besides quinia, separable from it, and having analogous chemical relations, they suggested that there might be a similar identity between their therapeutic properties, and inferred that it might be no less available as a febrifuge. The subject was accordingly investigated by Magendie, Gittermann, Chomel and others, who, after slight inquiry, rejected its pretensions as such an agent; the last-mentioned experimenter doing so after using it in one case only. After this extremely limited trial, little more attention was bestowed upon it, until inquiry was prosecuted with more vigour by Dr. Bally, in 1825, who succeeded in immediately checking twenty-five out of twenty-seven cases of intermittent fever, and even the other two yielded upon judicious perseverance in the same remedy. Other experimenters in Italy, France, and Germany, among whom were Mariani, Wutzer, Dufresne, Potier, and also Bardsley, of England, all reported in its favour, even when compared with quinia. In this country attention was specially directed towards the subject by Prof. Wm. Pepper (*American Journ. Med. Sciences*, January, 1853), who administered this substance with signal success, confirming all previous statements as to its efficacy, having promptly checked eleven out of fifteen cases of intermittent fever, and two of those remaining yielded to a second administration of the same febrifuge. The greater number of these cases were of many months' duration, attended with enlargement of the spleen, and more or less derangement of the general health, which would tend to make a successful result still more conspicuous.

The humble position reached by this article of the *materia medica* as a therapeutic agent, must not be attributed to the fact that it has been tried and found wanting, but rather to the tardiness of physicians in confiding in newly proposed medicinal agents. But another and more obvious reason is perhaps due to the fact that quinia has been found so effectual as a febrifuge, that there scarcely exists a hope of ever securing a more efficient one, and consequently so long as this can be readily procured, a substitute for it will meet with little attention. The demand for quinia has now not only increased for the cure of disease, but it is issued as a prophylactic to soldiers in the field, not only among our own in the Southern States, but among the armies of Europe stationed in the malarious regions of China, India, and Mexico. These increasing demands for consumption, and the non-increase but rather decline in supply of the material from whence it is derived, can of course have but one effect, that of making it more costly, and of urging us to seek an available substitute. In all

charitable institutions where it is desirable to reduce expense to the lowest point compatible with the object in view, an efficient substitute is urgently demanded. It was in view of this fact that I was induced to specially observe a certain number of well-defined cases of intermittent fever, presenting themselves at the Dispensary of the Howard Hospital, in hope that something positive could be ascertained as to the true value of the sulphate of cinchonia. The first case recorded was August 15th, and the last Oct. 25th, although during this interval there were not less than two hundred instances in the general register of the house, yet only those are specially recorded and embodied in this report as were well defined, and had been under no other immediate treatment. Where obscure cases afterwards assumed this character, or a more remittent form, the same agent was employed with equally satisfactory results. The epidemic was one of unusual violence and duration, many cases assuming a severe congestive form, with more or less visceral disturbance, but one of the most prominent features was the disturbance of the nervous system; the neuralgic symptoms were so prevalent, that not unfrequently, by their occurrence, the fever was anticipated some days before it assumed the decided form, and after the subsidence of everything connected with the febrile state, these general pains simulating rheumatism often appeared, not unfrequently affecting a special nerve or even one of its branches with a violent neuralgia, which yielded with the other symptoms to the antiperiodic.

1. *Mode of Experimenting.*—The frebrifuge was administered at the onset before it was fully ascertained whether the fever was about to steadily proceed with its paroxysms, or whether, on the other hand, it would spontaneously disappear of itself, but as the same course is pursued where the substance used is of another variety, it will be seen that the comparison does not present that variance which might at first be supposed.

2. *Use, Formulae, Mode of Administration, Duration of Use.*—In all instances the salt used was the disulphate of cinchonia, of known purity, directly from the laboratory. The smallest quantity given during a single intermission to arrest the paroxysms was five grains, to a child two years of age, suffering with a tertian form after having been troubled the entire summer with cholera infantum, and was in consequence much reduced in strength before the febrile condition appeared, with little appetite and irritable stomach. A slight purgative of hydrarg. cum creta was given as soon as the fever began to decline, then one and a half grain of the antiperiodic was administered every hour, until the above quantity had been taken. There was no return of the chill at the expected time, and a scarcely perceptible fever, probably due to some indiscretion in diet; from this time forward there was no return, although the general state of the system, which improved very slowly from the previous disorder, was one quite favourable for continuance of the disease. The maximum quantity used during a single

intermission was thirty grains, to a female aged 30 years, in doses of five grains every two hours; the only effect noticed aside from checking the paroxysms was considerable vertigo and buzzing of the ears, but no headache or other painful symptom. The largest dose given at one time was fifteen grains to a stout and apparently otherwise healthy man, three hours before the expected return of a paroxysm, which had been of unusual violence, lasting some hours, and succeeded by extreme gastric disturbance and general depression. He had previously experienced four attacks, each coming on at about 12 at noon, followed at 5 P. M. by the fever, which persisted during the night with active delirium until 6 the next morning, when general muscular pains harassed him until the hour for return of the succeeding cold stage. After a brisk purgative, which operated in two hours, the mentioned quantity of the febrifuge, suspended in tinct. lavand. c., was administered at once. This was followed by no nausea or other unpleasant symptom, except the fulness of the head which appeared about the expected time of return, but no chill or symptom of it was observed, except slight gastric uneasiness at the hour when vomiting had usually been troublesome. Three weeks afterwards there had been no return of the disorder, and he promised to visit us should another recur. In a female, aged 29 years, with a quotidian of one week's duration, giving rise to such disturbance of the system that she insisted upon immediate relief, and to effect this one scruple of the sulphate of cinchonia was given at two doses with an interval of one hour between them as soon as the febrile state declined. It was attended with no other disagreeable effect than the cerebral symptoms, which were not so distressing to the patient as those resulting from quinia, with whose properties in this respect she was familiar, having suffered each autumn from intermittent fever for some years past. The common dose for an adult was about three grains, repeated every hour until the desired quantity had been exhibited, which usually was one scruple. I now feel assured, however, that in many instances a less quantity will effect the desired result, but as this inference was drawn rather late, it was thought most judicious to continue as begun, that the relative effects between the different cases might not be thereby impaired.

As cinchonia is more soluble than any of the other salts obtained from barks, the most efficient mode of its administration was that of a solution with one of the mineral acids, usually the aromatic sulphuric, but it readily combines with tinct. ferri chlor., U. S. P., and in the proportion of two scruples to the ounce of the last may be used as a prophylactic in the dose of ten drops, in water, an hour before each meal. With organic acids it is no less soluble, and when desirable to combine with it the citrate or tartrate of iron, the citric or tartaric acids, respectively, will be found ready solvents. It may be given in pill or powder, but the solution is preferable. In using cinchonia in reference to the febrile state the same rule is to be followed as when quinia is prescribed, and in all cases an attempt was

made to begin its administration during the absence of fever, and so early that the last dose should precede the chill some two or three hours. This was the rule adopted, but, of course, in many instances it will be found impracticable, where larger doses at shorter intervals will be necessary, and in some instances the first portion was given during the declining fever of one paroxysm and the last at the commencement of the cold stage of another. In none did we observe the one prolonged or the other aggravated by such a course, and it has uniformly been our purpose to give the total quantity of the antiperiodic necessary during the intermission, instead of pursuing the course advocated by some of exhibiting certain quantities at stated periods until the commencement of the cold stage, then waiting until the succeeding intermission, and so on, until the desired effect is produced. In following this plan we have yet to see anything sufficient to cause us to pursue another. The duration of time over which the use of the alkaloid extended, varied, being discontinued as a usual thing as soon as the paroxysmal aspect was destroyed; it was then occasionally given at the end of six days to prevent a recurrence, as it is well known that all intermittents tend to return at the seventh, fourteenth, and twenty-first days. Hence a third of the original amount found necessary to arrest the progress of the paroxysms was repeated at each septenary period, and where this direction was carefully carried out, we do not remember more than two instances where a return was not prevented. One of these was a gardener, living in a marshy district, and when the quantity of the febrifuge was increased there was no return. The other was that of a female, aged 29 years, with a tertian of ten days' duration, which was expected to return at the stated day and hour, but it was very desirable to prevent, if possible, another paroxysm; five grains were given every hour until a scruple had been used; there was no return of the chill or fever. At the end of a week ten grains more were administered, but a paroxysm occurred the next day. A scruple in three grain doses was given to arrest the fever, which remained absent nine days, when it returned once more.

3. *General Accidents, Tolerance, etc. etc.*—Nausea and vomiting were observed to follow the use of this substance in five cases; two of these became more affected by continuing the dose, although one persisted in it after diminishing the quantity, and in the other no further attempt was made. The remaining three cases were children, in whom the gastric irritation was one of the most prominent and distressing symptoms, and as it soon subsided after an alkaline draught, it is scarcely proper, perhaps, to attribute it to the medicine.

Cephalalgia was quite prominent in six; one described it as acute in the frontal region, which was attended with a peculiar nausea, lasting some time, and returning after each dose; the cinchonia was not omitted on this account, but persevered in until all was used, after which there was neither return of the paroxysm nor headache. In another the

same symptom had previously occurred after the use of quinia, when it was more severe and enduring than after cinchonia. In reference to the peculiar assemblage of cerebral symptoms comprised under the term "cinchonism," it resulted in the majority of instances, but it was not observed that greater immunity was thereby secured in proportion as these signs were more marked or earlier evident. In one case the vertigo was so intense after twenty grains of this substance had been taken within ten hours, that the patient was unable to walk without falling, and she inquired if quinia was not the preparation given, as when this had been used by her on former occasions, the same effect had always been induced, but much more unpleasant from the severe pain attending it. This was remarked also by other parties.

The taste is not so bitter or durable as from quinia, and for this reason cinchonia can be administered to children where the former is stoutly refused. The impaired appetite and general feeling of *malaise* not unfrequently following the use of quinia, which to some is the most objectionable feature to its use, was not noticed to the same extent after cinchonia, and in some did not occur at all; on this account it may be preferred to other tonics of a similar character.

4. *Efficacy as an Antiperiodic.*—We previously remarked that the following cases, arranged for inspection in a tabular form, are those distinctly defined and recorded in reference to this feature alone; where the type is omitted and entered mixed, it is meant that at the beginning it was perhaps a quotidian, then merged into a tertian, and could not be so expressed without interfering with the assumed arrangement.

No.	Age.	Sex.	Type.	Number of paroxysms before treatment.	Quantity of cinchonia administered.	Number of paroxysms after medication.	Remarks.
1	20	Male	Tertian	Two	gr. xx.	None	
2	40	"	"	"	" xx.	"	
3	13	"	"	Three	" xv.	Two	
4	6	Female	Quotidian	"	" xv.	None	
5	23	"	"	One	" xx.	"	
6	25	Male	Tertian	Seven	" xx.	"	
7	23	Female	"	Five	" xx.	"	
8	20	"	"	Three	" xx.	One	
9	33	"	Quotidian	"	" xx.	None	
10	19	"	"	Eight	" xx.	"	
11	22	Male	Tertian	Four	" xx.	"	
12	28	"	Quotidian	Sixteen	" xx.	"	
13	16	"	Tertian	Three	" xv.	One	
14	8	"	Quotidian	Seven	" x.	None	
15	4	Female	"	Fourteen	" viij.	"	
16	6	"	Tertian	Two	" viij.	"	
17	40	Male	Quotidian	Six	" xx.	"	
18	5	"	Mixed	"	" x.	"	
19	36	"	Quotidian	Three	" xx.	Two	
20	11	"	"	Six	" x.	None	
21	8	"	"	Three	" viij.	"	
22	17	"	Tertian	Four	" xx.	"	
23	7	Female	"	Five	" x.	"	
24	60	Male	"	Eleven	" xx.	One	
25	20	"	Quotidian	Four	" xx.	"	
26	30	"	"	Three	" xx.	None	

No.	Age.	Sex.	Type.	Number of paroxysms before treatment.	Quantity of cinchonia administered.	Number of paroxysms after medication.	Remarks.
27	40	Male	Quotidian	Seventy	gr. xx.	None	
25	50	"	Tertian	"	" xx.	"	
29	55	"	"	Seven	" xx.	"	
30	14	Female	"	Twenty	" xv.	"	
31	28	Male	Quotidian	"	" xx.	One	
32	26	Female	Tertian	Seven	" xv.	"	
33	2	"	"	Six	" v.	None	
34	4	Male	"	"	" vi.	"	
35	32	"	Quotidian	Six	" xx.	"	
36	30	"	Tertian	Three	" xv.	"	
37	8	"	"	Six	" x.	"	
38	6	Female	Quotidian	Seven	" x.	One	
39	30	Male	"	Two	" xx.	None	
40	15	"	Tertian	Ten	" xv.	"	
41	30	"	Quotidian	Ten	" xx.	One	Severe neuralgia also.
42	15	"	"	Two	" xx.	Two	
43	30	"	Tertian	Three	" xx.	None	
44	40	Female	Mixed	"	" xx.	"	
45	35	Male	Quotidian	Six	" x.	"	
46	38	"	"	Fifteen	" xx.	"	
47	50	"	Tertian	"	" xx.	"	
48	11	"	"	Three	" x.	"	
49	50	"	Quotidian	Twelve	" xx.	"	
50	55	"	Tertian	Ten	" xx.	"	
51	3	"	Quotidian	Thirteen	" vi.	"	
52	18	Female	Tertian	Two	" xv.	"	
53	35	"	Quotidian	Seventy	" xx.	"	
54	40	"	Mixed	"	" xx.	"	
55	48	Male	Tertian	Three	" xx.	"	
56	37	Female	"	Two	" xxx.	"	
57	11	Male	"	Four	" x.	"	
58	15	"	Quotidian	One	" xx.	"	
59	50	"	Mixed	"	" xx.	Two	
60	46	"	Tertian	Seven	" xx.	None	Severe cephalgia after the cinchonia.
61	22	"	"	Two	" xx.	"	
62	18	"	"	Four	" xx.	"	
63	29	Female	Quotidian	Three	" xx.	"	
64	36	Male	"	Three	" xx.	One	
65	9	"	"	Seven	" xv.	None	Hepatic and splenic enlargement.
66	39	Female	Tertian	Six	" xx.	Several	
67	18	"	Quotidian	Eight	" xv.	None	Cinchonia without effect.
68	35	Male	"	"	" xx.	One	
69	22	"	Tertian	"	" xx.	None	
70	22	"	"	Three	" xx.	"	
71	19	"	Quotidian	Four	" xx.	"	
72	50	"	"	One	" xx.	"	
73	46	Female	Tertian	Four	" xx.	"	
74	10	Male	"	Three	" xv.	One	Chill was a slight one.
75	15	"	"	"	" xv.	Three	But none after.
76	16	Female	"	Four	" xv.	None	Cerebral symptoms very decided after the febrifuge.
77	58	Male	Mixed	"	" xx.	"	
78	15	"	Quotidian	Seven	" xv.	"	
79	13	"	"	Eight	" x.	"	
80	3	"	Tertian	Six	" x.	One	
81	8	"	"	Nine	" x.	None	
82	44	"	"	Seven	" xx.	"	
83	13	Female	"	Five	" xv.	"	
84	58	Male	"	"	" xx.	"	
85	48	Female	Quotidian	Five	" xx.	"	
86	8	"	"	Twelve	" x.	One	
87	23	"	Tertian	Six	" xx.	None	
88	28	Male	Quotidian	Five	" xx.	"	
89	15	"	"	Three	" xv.	One	
90	29	Female	Tertian	"	" xx.	None	
91	5	"	"	Two	" viii.	"	
92	28	Male	"	Six	" xx.	"	
93	35	"	"	Three	" xx.	"	
94	29	"	"	Nine	" xx.	One	
95	55	"	Quotidian	Twelve	" xx.	None	
96	9	Female	"	Two	" x.	"	
97	16	Male	"	Three	" xv.	"	
98	29	"	Tertian	"	" xx.	"	
99	30	"	Quotidian	"	" xx.	"	
100	5	Female	"	Seven	" x.	One	

The result thus calculated gives :—

Fevers cut short— <i>i. e.</i> , which have not presented a single paroxysm from the commencement of medication	79 per cent.
Fevers which have presented one paroxysm, but not two after the commencement of medication	15 "
Fevers which have presented two, but not more paroxysms	4 "
Fevers which have presented three or more paroxysms	1 "
Fevers which cannot be introduced into these categories, but must be regarded as not cut short.	1 "
	<hr/>
	100

It will be perceived that seventy-nine per cent. of the fevers were cut short after the administration of the febrifuge, and in those instances where a single paroxysm afterwards occurred, an examination of the preceding table will show that nine were of a quotidian form, and reference to the full notes in my possession show that in six of these, the use of the antiperiodic was delayed until there was not time to insure the requisite amount being taken before the hour for the occurrence of the chill, and had this not been the case, the first class would have perceptibly increased. In one case only was it found that the sulphate of cinchonia was without effect in sooner or later arresting the progress of the disease.

5. *Relapse.*—In preventing this we did not find cinchonia less efficacious than quinia, and when care was taken to give a certain portion at the time a return might be expected, it was effectually prevented; but as to the precise proportion in which the relapse would have occurred we have no positive means of knowing, since those affected were of the usual class of outdoor patients, with others frequently dependent upon them for support, and living in the outskirts of the city, constantly exposed to malarial emanations, and that all danger of a return might be avoided as much as possible, it was deemed best, under the circumstances, to place them upon the use of tonics, etc., so that any conclusion is quite unreliable upon this point.

*General Deductions.*—In several of the above instances quinia had been used with the effect of arresting the progress of the disease for a time, until the approach of one of the septenary periods, when the paroxysms returned to the number shown in the column, and in more than one case this occurred two or three times, which was not the case after administration of cinchonia. Undue importance must not be attached to this fact, causing us to draw the inference that the relative value of cinchonia is *greater* than that of quinia, but rather to the attention given to recuperation of the general health and abatement of the epidemic influence. But an extensive use of both substances justifies the statement that, in slightly larger doses, cinchonia is equal as an antiperiodic to quinia; so much so, that, in private practice where either can be procured, I order the former with as much assurance of

success as if the latter were used. It is more soluble ; tends less to derange the gastric functions ; begets less of the malaise ; the cephalic symptoms are less violent and enduring, and it is not followed by any special unpleasant effect more than is observed to ensue after use of quinia, and it may be administered in all cases and under all circumstances where this substance is indicated. In saying this, we do not profess to have observed anything new in its mode of use, administration, or the effects arising from it, more than previously detailed by Bally, Bardsley, Pepper, and others who have impartially investigated its properties ; but after a more extensive series of experiments, especially in intermittent fever, we can confirm the results obtained by them.

In conclusion, we hope that others will be prompted to extend to it the careful consideration demanded by the subject, and doubt not but all said in its favour will in essential particulars be confirmed.

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ART. IX.—*Miasmatic Typhoid Fever.* By JAMES J. LEVICK, M. D., one of the Physicians of Pennsylvania Hospital. (Extract from a paper read before the Philadelphia County Medical Society, October 14, 1863.)

Without discussing the question of the identity or non-identity of typhus and typhoid fevers, I propose briefly, in this paper, to direct attention to some of those modifications of typhoid fever which are developed by the peculiar antecedents of the individuals thus affected. Reference is not now made to those cases which, from some personal idiosyncrasy, present occasional peculiarities, such as may be seen in the walking cases of this disease, or in those instances in which the cerebral or pulmonic symptoms are so prominent as to mask the ordinary enteric phenomena ; but to those in which there is associated with the ordinary cause of the disease a miasmatic or other specific poison, the coexistence of which superadds to the ordinary symptoms of the disease, phenomena of its own production. I do not mean by this to imply that necessarily a hybrid disease is produced ; but believe that in some instances, at least, the two diseases run their course together, side by side, to some extent modifying each other, but not inevitably losing the individuality of either.

This doctrine of the coexistence of specific morbid poisons is in direct opposition to the teachings of the earlier writers. John Hunter distinctly states that "no two fevers can exist in the same constitution, nor two local diseases in the same part at the same time." That this opinion of Hunter is erroneous has been clearly demonstrated by Ring, by Marson,